

THE CLINICAL CHARACTERISTICS OF CELIAC DISEASE IN CHILDREN AT THE TIME OF DETECTION

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Objective - The aim of this study is to analyse the clinical characteristics of celiac disease at the time of its detection in relation to the age of the patient.

Subjects and Methods - Through examining the medical documentation of patients with celiac disease from the Department of Paediatrics in Tuzla (January 1st 1995 to March 31st 2011), the clinical symptoms and signs of the disease were analysed. The diagnosis of celiac disease was established on the basis of the criteria prescribed by the European Society for Pediatric Gastroenterology Hepatology and Nutrition. The subjects were divided into three groups: ages 0-1.9; 2-10.9, and 11- 14.9 (younger, middle, older), and, depending on the particular type of celiac disease, into groups with typical or atypical forms of the disease. The results are presented in the form of absolute and relative numbers.

Results - Seventy-two subjects were examined. The typical form of the disease was found in 46 subjects (26 girls and 20 boys), while the atypical form was found in 26 subjects (21 girls and 5 boys). In subjects with the typical form of the disease the main symptoms and signs in all age groups included: frequent stools, loss of body mass (BM), loss of appetite and paleness of skin. BM lower than the 25th percentile in the older age group was found in three children, while a body mass index (BMI) below the 25th percentile was found in more than half of all the subjects. In subjects with the atypical form of celiac disease, paleness of skin was the most common clinical sign for all three groups. Loss of body mass was found in more than half the subjects in all three age groups. BMI below the 25th percentile in the younger group was found in six subjects, while in the older group there were only three. BMI below the 95th percentile was found in two children from the older group.

Conclusion - The most common signs of the disease among the children with the typical form of the disease included, regardless

of age, the following: frequent stools, loss of BM, loss of appetite and paleness of skin. In the atypical form of the disease the most common sign of the disease in all three groups was paleness of skin, while a BMI higher than the 95th percentile was found in two children, which implies the necessity of considering celiac disease in cases where there are no clinical symptoms or signs of malabsorption.

Key words: Celiac disease ▪ Clinical signs and symptoms ▪ Children

Introduction

Celiac disease (gluten enteropathy) is a chronic disease which usually attacks the proximal parts of the small intestine, which is caused by an inadequate immune reaction in contact with gluten in genetically predisposed persons. The main characteristics include: permanent glutene intolerance, various levels of (both morphological and functional) impairment of the mucous membrane in the small intestine, as well as a number of various clinical symptoms, not all of which are consequences of malabsorption. Removing gluten from the diet leads to the absence of the histological and clinical signs of the disease, while its re-introduction causes a relapse of the intestinal histological changes, while the clinical symptoms may not necessarily return (1). The disease occurs among both children and adults, but the "classic" clinical features occur more frequently during the first few days of life (2).

Celiac disease is one of the most frequent known genetic diseases with a prevalence of 1% - 2% in the general population (3). The clinical features of celiac disease are not uniform and are primarily dependent upon the form of the disease, as well as the age of the child with the disease. Thus infants and younger children will tend to manifest symptoms which are typical of celiac disease, while in most children and adolescents extra-

intestinal manifestations will be dominant, or the symptoms will be completely absent (4).

The typical form of celiac disease usually becomes apparent between the 7th and 24th month of a child's life, most often after the introduction of floury foods into the infant's diet. Stools are profuse, foamy, greasy and smelly. The intestines are meteoristic, while the wall of the stomach is hypotonic and hypotrophic, which leads to the manifestation of a large, lymphatic belly that is in particular contrast to the otherwise skinny body. The occurrence of oedema is due to hypoproteinemia. Due to anaemia, which occurs in 20%-40% of children suffering from celiac disease, there is also paleness of skin and mucous membrane (1, 5).

The atypical form of the disease usually occurs in early phases of infancy, after the introduction of gluten into the diet, or after the second year of life. The most common symptoms pertaining to the gastrointestinal tract are recurring abdominal pains, recurring diarrhoea that alternates with constipation. Older children and adults usually have symptoms unrelated to the gastrointestinal tract, such as growth retardation, neurological symptoms or symptoms and signs of anaemia (6). Although the children suffering from the atypical form of celiac disease also suffer from malabsorption, cases have been reported pertaining to this form of celiac disease of children with BMI >95th percentile (7).

The purpose of this study is a retrospective study by an analysis of the clinical characteristics of celiac disease in relation to age.

Subjects and Methods

By means of a retrospective study the medical documentation was analysed from the Department of paediatrics in Tuzla of patients ages 0 - 14.9 diagnosed with celiac disease between January 1st 1995 and March 31st

2011. Celiac disease was diagnosed on the basis of the criteria issued by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN): significant clinical and laboratory improvement after the introduction of a strict gluten-free diet; specific results for celiac disease upon biopsy of the small intestine while the patient was on a normal diet; finding of circulating IgA antibodies to gliadine and fibrous transglutaminases for determining the total serum IgA; the disappearance of antibodies due to a gluten-free diet, and HLA typization (8, 9).

At the time of detecting the disease, the following clinical parameters were analysed: anamnestic data regarding the occurrence of frequent stools, loss of appetite and body mass, vomiting, abdominal pain, growth retardation, irritability, and during the physical examination, body mass (BM) and body height (BH), body mass index (BMI), the existence of an enlarged abdomen, and the presence of oedema. The subjects were divided into three groups according to their age: ages 0 to 1.9; ages 2 to 10.9, and ages 11 to 14.9, further called the younger, middle, and older groups, and into two groups in relation to the type of celiac disease: subjects with the typical or atypical form of the disease.

The subjects were ascribed with their particular form of celiac disease based on two or more of the following criteria: anamnesis with symptoms of chronic diarrhoea, loss of BM, abdominal pains and abdominal distension, vomiting, irritability, BM <25th percentile and BH <25th percentile, paleness of skin with anaemia confirmed by laboratory tests and the presence of oedema (10), while the atypical form of celiac disease was ascribed to those subjects who met two or more of the following criteria: anamnesis with no symptoms of chronic diarrhoea, chronic constipation (stool frequency <3 stools per week), inexplicable growth retardation (small height

with BH <3rd percentile for the particular age), anaemia, rickets, recurrent aphthous stomatitis, abdominal distension (11, 12).

The age of the subjects has been given in the form of their decimal age in years based on the decimal calendar, i.e. between the date of birth and the date of examination. The results are presented in absolute and relative numbers.

Results

The analysis included 72 subjects, of which 46 or 63.8% (26 girls and 20 boys) had the typical form of celiac disease. They were aged from 0.5 to 14.6 years (± 7.1). The atypical form of the disease was found in 26 or 36.1% subjects (21 girls and 5 boys) aged from 0.5 to 10.6 years (± 6.6).

Table 1 shows the frequency of the main symptoms and signs of the typical form of celiac disease in relation to age at the time the disease was discovered.

Frequent stools, loss of body mass, loss of appetite and paleness of skin were the main symptoms and signs of the disease in all age groups. Abdominal pain and irritability in the younger age group were found in 18 children, while all three children from the older age group had these symptoms. Body mass below the 25th percentile was also found in all three children in the older group, while BMI below the 25th percentile was found in more than half the subjects in all three examined age groups. No child with the typical form of celiac disease in any of the three age groups was noted to have BMI higher than the 95th percentile. The presence of oedema was noted in 40% of subjects in the younger age group, as well as 21.7% of the middle age group, while no child from the older age group was noted to have this clinical sign.

Table 2 shows the frequency of the main symptoms and signs of the atypical form of celiac disease in relation to age at the time of discovering the disease.

Table 1 Frequency of symptoms and signs of the typical form of celiac disease at the time of discovery

Symptoms and signs	Age groups (years)							
	0 - 1,9 (n=20)		2-10,9 (n=23)		11-14,9 (n=3)		Total (n=46)	
	n	%	n	%	n	%	n	%
Frequent stools	20	100	22	95.6	3	100	45	97.8
Loss of body mass	20	100	22	95.6	3	100	45	97.8
Loss of appetite	20	100	21	91.3	3	100	44	95.6
Vomiting	13	65	14	60.8	2	66,6	27	63
Abdominal pain	18	90	14	60.8	3	100	30	68.1
Irritability	18	90	11	47.8	3	100	15	76.1
BM < 25th percentile	12	60	16	69.5	3	100	31	67.4
BH < 25th percentile	1	5	9	34.6	2	66,6	12	26.1
Paleness of skin	20	100	23	100	3	100	46	100
Enlarged abdomen	15	75	12	52.2	3	100	30	65.2
*BMI < 25th percentile	14	70	12	52.2	2	66,6	28	60.8
*BMI > 95th percentile	-	-	-	-	-	-	-	-
Presence of oedema	8	40	5	21.7	-	-	13	28.2

*Body Mass Index

Table 2 Frequency of symptoms and signs of the atypical form of celiac disease at the time of discovery

Symptoms and signs	Age groups (years)							
	0 - 1,9 (n=7)		2-10,9 (n=11)		11-14,9 (n=8)		Total (n = 26)	
	n	%	n	%	n	%	n	%
Frequent stools	-	-	-	-	-	-	-	-
Loss of body mass	4	57.1	8	72.7	7	87.5	19	73.1
Loss of appetite	7	100	5	45.4	1	12.5	13	50
Vomiting	2	28.5	2	18.1	3	37.5	7	26.9
Abdominal pain	4	57.1	5	45.4	3	37.5	12	46.1
Irritability	5	67.1	7	63.6	4	50	16	61.5
BM < 25th percentile	4	57.1	5	45.4	2	25	11	42.3
BH < 25th percentile	2	28.5	4	36.3	2	25	8	30.7
Paleness of skin	7	100	10	90.0	8	100	25	96.1
Enlarged abdomen	5	67.1	7	63.6	4	50.0	16	61.5
*BMI < 25th percentile	6	85.7	5	45.4	3	37.5	14	53.8
*BMI > 95th percentile	-	-	-	-	2	25	-	-
Presence of oedema	-	-	-	-	-	-	-	-

*Body Mass Index

None of the three age groups included children with frequent stools or oedema. Paleness of skin was the most common clinical sign for all three age groups involved. The loss of body mass in the younger group was

found in four children; in the middle group it was found in eight children; while seven of the subjects from the older age group presented this symptom. Body mass lower than the 25th percentile in the younger age

group was found in four children, and five children in the middle group, while only two children from the older group had this symptom. Body mass index lower than 25 in the younger group was found in six out of seven subjects, while the older age group only included three children. Two children from the older age group were noted to have BMI above the 95th percentile.

Discussion

During our study we noted that frequent stools, loss of BM, loss of appetite and paleness of skin were some of the main symptoms and signs in all age groups of children suffering from the typical form of celiac disease. Irritability and abdominal pain were found in more than half the subjects from all age groups. The high percentage of children with oedema (28.2%), confirmed by laboratory tests in the form of low values of albumin, is not a usual result for children with celiac disease. This may be explained if we assume that the disease had already been present for a longer period before it was diagnosed. The reasons for such a high rate of typical symptoms of celiac disease in all age groups are based on the fact that in the case of the majority of patients the suspicion of celiac disease was established on basis of the gastrointestinal symptoms typical of this disease.

In a study performed in Turkey by Demircen et al. it was noted that the most common symptoms of the typical form of celiac disease included: diarrheic stools (66%), loss of body mass (56%), abdominal pain and an enlarged abdomen (55%), while growth retardation was noted in 44% cases (13). Cataldo et al. found that the most common symptoms and signs among children suffering from the typical form of celiac disease included frequent diarrhoea and loss of body mass (90%), while enlarged abdomen and vomiting were found in 87% of those suffering from

the disease (14). The results of the study performed by Demircen et al. (13) correspond to the results found by Cataldo et al. (14) in Italy, which is also confirmed by the results of our study about the most common symptoms and signs of the typical form of celiac disease in all age groups.

The explanation that two children in the older age group experienced growth retardation probably has to do with the time of the development of the disease before it was diagnosed as celiac disease. In following the growth of these children after establishing the proper diagnosis and the beginning of treatment, it was noted that these children started growing rapidly, which shows that the main cause of growth retardation was the belated diagnosis of the disease. Similar results were seen by Barera et al. (12), who noted that the values for BM, BH, and BMI in children who were newly diagnosed with celiac disease were statically significantly lower than in the control group, which consisted of healthy children. However, the statistically significant diminishing of the values for these parameters was noted after a certain time period after the diagnosis was established among non-treated children who had not been keeping to their gluten-free diet (15). These results correspond to the results established in our own study.

As for the atypical form of celiac disease, no children were noted to have frequent stools or oedema. Paleness of skin was one of the most common clinical signs in all three age groups involved, and it was established as a sign of the disease through laboratory signs of anaemia. Through a retrospective analysis of the medical histories of children with the atypical form of celiac disease it was shown that there was not enough data regarding gastrointestinal symptoms. The most common parameters which pointed to the atypical form of the celiac disease included clinical signs of paleness, loss of BM, and

irritability. In our study we noted as many as two children whose BMI was above the 95th percentile, which is also confirmed by the results of study in some other studies (16, 17).

According to the study conducted by Sharma et al. in a study in India, out of a total of 42 children, 18 subjects suffered from the atypical form of the disease. The children with the atypical form of celiac disease were older than average at the time the diagnosis was made (10.4 ± 5.5 years), as opposed to children with the typical form. According to these results, the most common symptoms and signs in children with the atypical form of celiac disease included: absence of stool, enlarged abdomen, anaemia, and growth retardation (11). In a study conducted in Canada on a group of children who were grouped in the atypical group at the time of diagnosis, the most common symptoms included abdominal pain (90%), loss of body mass (71%), vomiting (53%), irritability (37%), and paleness of skin (40%) (18). The results of study conducted by Sharm et al. (11) and Rashid et al. (18) are partially in line with the results obtained through our study.

In a 21-year study conducted by Ravikumar et al. (19) in England between 1983 and 2004, a significant increase in the number of children with celiac disease was noted (from 11 children with the disease between 1983 and 1989, to 50 children in the period between 1999 and 2004). This study showed a dramatic decrease in the number of affected children with typical gastrointestinal symptoms, so that out of the 50 children suffering from celiac disease between 1999 and 2004 the majority had symptoms which were characteristic of the atypical form of celiac disease (19).

Since our study was a retrospective one, the results of the study imply that the per-

centage of the children with the atypical form of celiac disease was lower than the typical, which is not in accordance with the results of studies conducted elsewhere in the world. According to most authors, the ratio between the atypical and the typical forms of celiac disease is 5-7:1 (20). The results of our study can be explained by the fact that the diagnosis of celiac disease in the Clinic for Children's Ailments between 1995 and 2000 was established solely on the basis of anamnestic data, clinical examination and the results of non-specific malabsorption tests. After the introduction of serological celiac tests, and screening in high-risk children suffering from type 1 diabetes mellitus and Hashimoto thyroiditis, this ratio altered significantly in favour of the atypical form.

Conclusion

Our study shows that the majority of children with celiac disease suffered from the typical form regardless of age group. Frequent stools, loss of body mass, loss of appetite, and paleness of skin were some of the main symptoms and signs of the disease. As for the atypical form of celiac disease, the paleness of skin confirmed by laboratory tests as resulting from anaemia, was one of the most common clinical signs in all three participant age groups. The BMI higher than the 95th percentile noted in two children implies the necessity of considering celiac diseases even in cases where there are no clinical symptoms or signs of malabsorption.

Conflict of Interest: The author declares that she has no conflict of interest. This study was not sponsored by any external organisation.

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